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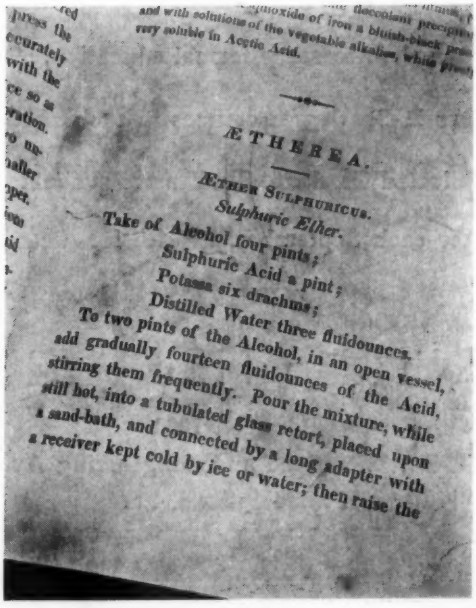

ÆTHEREA.

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Sulphuric Ether.

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Sulphuric Acid a pint;
Potassa six drachms;
Distilled Water three fluidounces.

To two pints of the Alcohol, in an open vessel, add gradually fourteen fluidounces of the Acid, stirring them frequently. Pour the mixture, while still hot, into a tubulated glass retort, placed upon a sand-bath, and connected by a long adapter with a receiver kept cold by ice or water; then raise the

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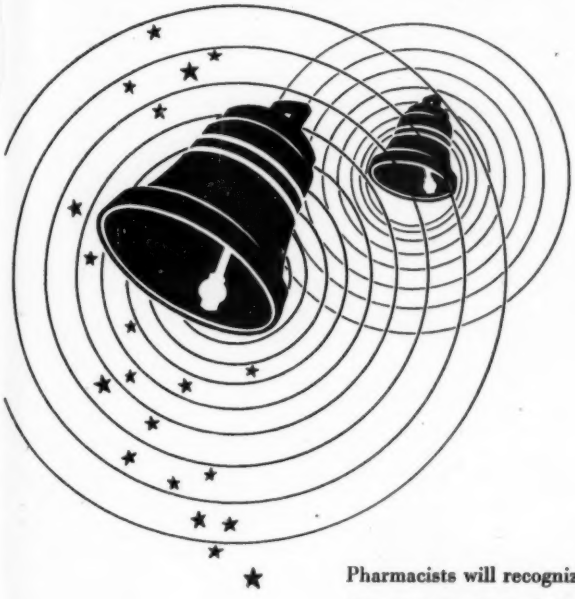

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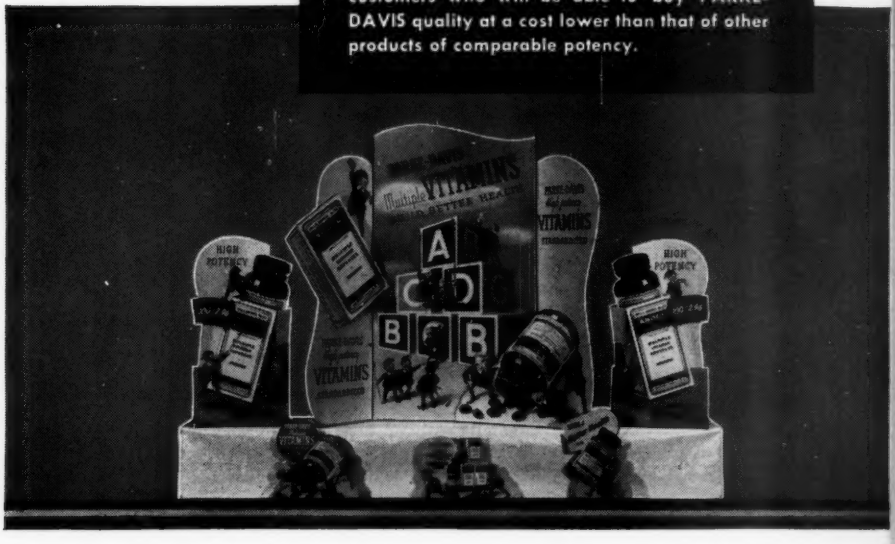

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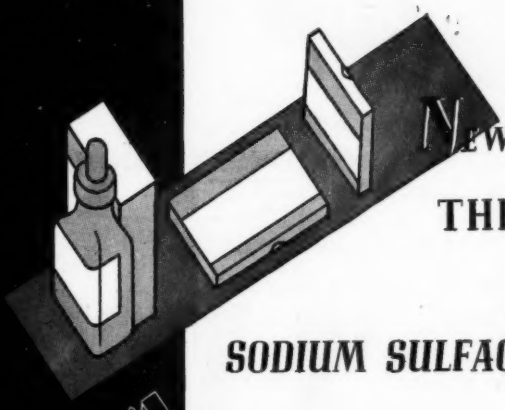

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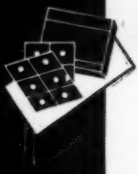

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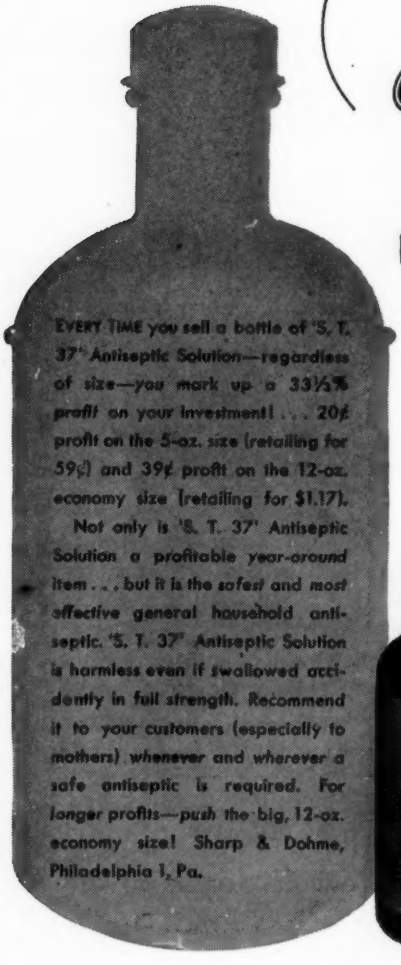

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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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CONTENTS

PAGE

Editorial:

Anesthesia 336

Articles:

The Battle for a Better Food and Drug Act. By T. Swann Harding 338

A Résumé of Selected Papers Presented Before the Scientific Section of the American Pharmaceutical Association 360

Selected Abstracts 373

EDITORIAL

ANESTHESIA

ON October sixteenth, this year, the one hundredth anniversary of the first use of ether in surgical anesthesia was celebrated. On this day in 1846 W. T. G. Morton, a dentist, demonstrated to a group of physicians at the Massachusetts General Hospital that ether possessed the remarkable property of making patients completely unaware of pain due to major surgery.

It is noteworthy that both the American Society of Anesthesiologists and the New England Society of Anesthesiologists honored Morton and commemorated his achievement with a three day meeting devoted to the advances in this highly specialized field of medicine. The accomplishments of the modern expert in anesthesia are truly remarkable. It is today almost of as much benefit to the prospective surgical case to exercise careful judgment in the selection of a competent anesthesiologist as it is to choose a good surgeon, although this fact is commonly ignored by both physicians and the laiety. Physicians are well aware of the fact that only too often an otherwise successful operation fails because of some accident due to anesthesia.

There is one all too common error in the immediate presurgical care of a patient. Most individuals, particularly those who never before have been anesthetized, regard an impending serious operation with almost the same degree of panic as if they were to be hanged. It is of slight comfort to these patients to assure them that "everything will be all right." Only the devout Christian is fully prepared emotionally to face the ordeal regardless of its outcome.

To many patients the trip to surgery is a most distressing ordeal and not much less harrowing than that uncivilized punishment meted out by organized society and known as capital punishment. For years now we have prided ourselves in a complete conquest of physical pain, but are we not somewhat callous from the standpoint of mental trauma? The psychiatrists tell us that mental agony can be just as devastating to the individual as physical pain and yet in many

cases its elimination is regarded as totally unnecessary or a luxury reserved only for the few who insist upon it.

We have today in the group of barbiturates drugs which by oral or parenteral use induce deep hypnosis and which then eliminate completely all knowledge of the trip to the operating room and its attending excitement. Much less inhalation anesthetic is then required and the patient recovers from the whole procedure with no knowledge of having left his hospital bed. This is humane and ideal anesthesia and wherever possible it should be the regimen employed. Obviously some cases cannot be so handled, but far more patients could be saved from the entire ordeal of an operation, excepting convalescence, than is now the case.

We have come a long way from those days when the pain of childbirth was deliberately unmitigated on the specious argument that it was God's will that woman should suffer in penance for the original sin. We still have progress to make, however, and on this anniversary of Morton's great contribution no better tribute could be paid him than a concerted effort to make anesthesia such an uneventful and even pleasant experience that it would lose all of the objectionable and even fearsome aspects with which it is now regarded by most who have experienced it.

L. F. Tice.

THE BATTLE FOR A BETTER FOOD AND DRUG ACT

By T. Swann Harding

ON March 31, 1938, the Wheeler-Lee Act was signed, broadening the power of the Federal Trade Commission to deal with all types of unfair commercial practices, and giving it new power to control false advertising. It specifically gave the Commission power to prevent the false advertising of foods, drugs, cosmetics, and healing devices. A false advertisement was defined as one "misleading in a material respect." Intent to defraud or injury to health must be proved to bring criminal provisions into operation.

On June 25, 1938, the Federal Food, Drug, and Cosmetic Act became law. It had been falsely called the "Tugwell Bill," more correctly the Copeland Bill. It is the present law under which the Food and Drug Administration, Federal Security Agency, operates, and its provisions are sufficiently well known not to require restatement here in what purports to be a partial account, at least, of the great battle which preceded its passage. Who opposed such laws as the above? Who favored them, and why, and how?

No proposition is, *per se,* either right or wrong. It is right or wrong, good or bad, for certain purposes, as related to certain situations, in the view of certain organizations or institutions, or as regarded by certain individuals or associations of individuals. The habitual associations of a person—religious, scientific, political, moral, commercial, medical, pharmaceutical, advertising, or what not—in the end very largely determine what that person will regard as good or bad. We therefore face a complex of cross currents and mutually conflicting propagandas when we seek to analyze the opinions which favored or opposed Federal regulation of proprietary remedies or what are commonly miscalled "patent medicines."

Even at the extremes there is no unanimity. Those grouped together in the opposition did not see eye to eye; neither did those grouped together as favorable to a more rigid drug law. The group commonly called the "unscrupulous" manufacturers and advertisers consisted of individuals who did not desire themselves, their friends,

or their relatives to be swindled, and who announced that they favored protection of the public health and pocketbook in all cases.

Each such individual, institution, and organization felt bound to assert adherence to the broad, basic principles that only harmless remedies should be sold for self-medication, that truth should rule in advertising, and that fraud should be suppressed ruthlessly. These people all wanted better patent medicine regulation, *but they wanted it strictly on their own terms,* i. e. they desired such regulation as would hit their "unscrupulous" competitors, but would leave them unmolested. For "they" always represented a particular case of immune virtue urged on to iniquity only now and then by the devious practices of evil competitors.

On the other hand all sorts of opinions existed among those who stressed the urgent necessity for better patent-medicine and drug-product regulation. Physicians as a class are interested in making it hard for quacks, tightening up standards of medical practice, discouraging self-medication after self-diagnosis, and protecting the so called "ethical specialties" which are, in reality, the doctors' own patent medicines. Ethical pharmaceutical manufacturers wish legislation that will bring their competitors to fair-trade terms.

There were and are marked differences also among the "bureaucrats"—the legal, technical, medical, and scientific employees of the Federal Government who have to enforce any new law enacted. There was marked cleavage at times between two Government institutions, the Federal Trade Commission and the Food and Drug Administration, as to which should regulate advertising, with the former winning out, but—and perhaps because—less well equipped technically to do so.[1] Much bitterness was engendered in this controversy and the process of legal enactment slowed down accordingly. Experts within the Government also exhibited wide diversity of opinion as to what kind of law to recommend, the extent to which regulation should go, what could reasonably be attempted—and so on.

In a democracy an effort must be made somehow to reconcile all such marked differences of opinion and to settle upon something that is sufficiently agreeable to all to be enacted into law. This is very difficult because so much expression of opinion amounts to pure propaganda and is couched in meaningless generalized terms. Real motives are cloaked in empty verbalization.

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[1] Yet FTC has done such a good job of enforcing its law as to disappoint any who expected it to be lenient.

Those determined to have a new law must therefore speak in general terms also, seeking deliberately to make their statements mean different specific things to different individuals, groups, or organizations. They must seek, as St. Paul once advised, to be "all things to all men," i. e. to get each group to believe that it will gain more than it will lose by the passage of a "better" drug law. This is a long and arduous process.

On the basis of what happened after the miscalled "Tugwell"[2] (really Copeland) Bill was first introduced in Congress, we shall seek here all too briefly to analyze the propaganda related to passage of a revised food and drug law, limiting ourselves to drug products. Broadly speaking the opposition to improved legislation passed through three phases:

1. It was arrogantly opposed to the passage of any new law at all, and simply stormed in protest; 2. it realized that the pressure was too strong, consumers were too much aroused, that the passage of some sort of legislation was inevitable, and it therefore proposed bills which looked strong, but were in actuality weaker than the existing (1906) law; 3. it discovered that there was dispute between two Government units, each of which desired to regulate advertising and, believing that the Food and Drug Administration would be far more strict than the Federal Trade Commission, a belief somewhat belied in recent years, it supported the latter's bill. Finally, advertising regulation was placed in the Commission's hands. As a last resort the opposition sought to emasculate the Food and Drug Administration's bill.

The propaganda relative to these various revised food and drug bills split nine ways. We must take up each classification separately.

1. *The "Unscrupulous" Drug Manufacturers.* This may be called the "patent medicine ring," or whatever you like. The reference is to those makers of trademarked products for self-medication who wished to have the greatest possible latitude in advertising and in recommending their products that was consistent with good financial return. When considering them we must remember that the original Harvey W. Wiley Food and Drugs Act was not primarily consumer legislation—however Dr. Wiley himself may have seemed to regard it at times. It was undoubtedly presented as such a measure to spe-

[2] So called by many who wished to damn it by attaching Rexford Guy Tugwell's name to it. Tugwell did vigorously advocate passage of such legislation.

cial groups, but trade and commerce knew it as one of a number of measures proposed thirty or forty years ago to ensure fair trade practice and to abolish "unfair competition in trade."

After the bill became law, Dr. Wiley himself formulated a regulatory policy designed to accomplish the purposes of the act with as little disturbance to business as possible. This he himself told New York commercial interests. (See *Oil, Paint & Drug Reporter,* Sept. 14, 1906.) Only gradually, as consumer education expanded and consumer pressure groups appeared, did the 1906 law come to be regarded as of primary benefit for consumer protection. The regulatory policy changed accordingly. By 1934 a trade journal was warning the drug and cosmetic industry that representatives of the United States Food and Drug Administration are "a group of people prejudiced in the interests of the public. These officials are most apt to lean too far in that direction." (*Drug and Cosmetic Industry,* May, 1934.)

But, in 1933, the United Medicine Manufacturers of America announced themselves as ready to fight the proposed revision of the Food and Drugs Act. They declared, of course, that consumers must be protected from injury to health and from fraud, for no one dared defy the consumer then. They wanted the unfair competitor brought to terms. But, they asserted—and quite dishonestly—this new legislation deprives the public of its inalienable rights to self-diagnosis and self-medication. Quite as dishonestly they asserted that advertisements would be censored and prohibited without even being proved false. The aid of the press must be enlisted against the Bill by harping upon imminent loss of advertising revenue. (*Drug Trade News,* Sept. 18, 1933.)

The Drug Institute, the Proprietary Association, and the National Association of Retail Druggists were to be lined up in opposition. Newspapers and periodicals were to be brought to terms by exerting pressure through threats to cut advertising appropriations. The public was to be told, untruthfully, that the law, when passed, would require them to get doctor's prescriptions for their simplest needs and most trivial ailments.

The method worked in detail like this: A St. Paul concern selling food products, flavoring extracts, home remedies, toilet articles, spices, mineral well crystals, etc., sent out circular letters to their dealers asking them to protest against one form of the bill called S. 2000. They were to do so because passage of this bill would abolish

their business, prevent local dealers from earning a living, compel everybody to go to a doctor and pay a prescription fee for a headache remedy or for aspirin, make it illegal to buy home treatments for slight ailments, and put physicians in control of the sale of drugs.[3]

All of this was exaggerated. A great deal of it was nonsense. Much of it was positively false. Not even the American Medical Association itself would abolish home remedies and self-medication for minor ailments. In fact, it is on record to the contrary. (See Dr. Arthur J. Cramp, "Patent Medicines and the Law"—*American Mercury,* Nov. 1933; *Journal American Medical Association,* ix:671, March 1, 1913.) Furthermore the association had been dissatisfied with every bill presented and had persisted in writing bills of its own which ran little chance of passage, because they appealed mainly to doctors. However, your local dealer now sat himself down and indicted an epistle to the President in which he endorsed the letter and its sentiments.

In October, 1933, W. P. Jacobs of the Institute of Medicine Manufacturers (See Ruth Lamb's *American Chamber of Horrors*) assailed the new food and drug bill before an advertising women's luncheon as placing Government in undisputed control of private enterprise and setting bureaucrats above the law. He also declared that its passage would increase the cost of medical care which was already too high. Reputable manufacturers would be humiliated. Of course advertising could be improved a little, but there was nothing radically wrong with it. (New York *Herald-Tribune,* Oct. 25, 1933.)

This is almost pure mendacity. No proposal was ever made in any bill to set up dictatorial authority over medicine manufacture in the Department of Agriculture. No bill ever contemplated setting a bureaucrat above the law. Indeed the stringent bill then proposed did little more than embody in the law provisions based directly upon the language of the courts used in interpreting the existing law, and add to it other provisions suggested by those in charge of enforcing the Food and Drugs Act from 1917 on. Basically this group of individuals preferred to maintain their business in *status quo,* even if this did involve some deception of the public and considerable risk to the public health.

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[3] See *Popular Practice of Fraud,* T. Swann Harding, for details on this and confirmation of other facts presented herein.

2. *The Ethical Pharmaceutical Manufacturers.* This group and its propaganda may be considered more briefly. This is a fluid compartment, for the most ethical pharmaceutical manufacturers are also quite generally engaged surreptitiously in the manufacture of patent medicines, for others to purvey under their own labels. The usual method is for some avowed patent medicine concern to send these ethical companies orders for so many gallons, or hundred gallons, of such-and-such a formula. The formula or prescription made up is that for a so-called patent medicine.

Few true patent medicines exist. What is more common is for a maker or finisher of such products to find a formula or prescription in a book, or to devise a "new" one by making some changes in an old one, to secure a trade mark on the product, and then advertise and sell it as recommended to cure or remedy this or that. All such formulas are known to medical science; most of them either have been discarded by scientific medicine or else are used only in particular cases and under specific conditions. It is the name, not the formula, that is of value, and that name is made valuable by advertising.

Ethical pharmaceutical houses regularly engage in making up formulas for small concerns. The product is sent out in bulk under a general label. The final packaging, labeling, advertising, and selling is undertaken by the smaller concern which thus accepts the onus for "unethical" conduct. The ethical house also, in some instances, manufactures proprietaries which are advertised only to and dispensed only by physicians. These amount to doctors' patent medicines.

But the general nature of the business they conduct renders these ethical pharmaceutical manufacturers more scrupulous about outward appearances. They must make greater show of scientific control and of carrying on valuable research.[4] They must appear to advocate better drug regulation sometimes to such an extent as to drive them into opposition with their customers' financial interests. But the customers usually understand—and pardon such deflection into solicitude for the public welfare.

3. *The Advertising and Publishing Industries.* In this as in the two previous classifications were many individuals and groups usually

[4] Of course many of them do carry on research of extremely high quality as a matter of regular policy.

regarded as "enemies" of better food and drug legislation. This does not mean that they were conceived in sin, born in iniquity, and never deviated therefrom. These people also were respectable and upright citizens whose ideas and attitudes had been determined by the patterns of culture imprinted upon them by their organized activities and their associations.

In a broad way advertising controls the press and periodical publication industry in this country. Except in times of emergency, like that supervening when a new food and drug bill appears, this control is exercised with considerable sympathy and discretion. Emergencies draw lines tighter. Fear leads to more direct, dictatorial methods of control. Even then many advertisers and advertising agencies realize that "every knock is a boost," even when the knock is that of some putative consumer pressure group or is delivered by some public-spirited government official.

The general idea is to go just as far as possible in the matter of misleading or deliberately false advertising as can be gone without utter destruction of buyer confidence. Thus truth merges into "trade puffs," "trade puffs" lead to partial or misleading statements, actual deception and dishonesty follow in train. One thing leads to another and, during an economic depression, this occurs very rapidly, the trail leading down into the swamp of competitive mendacity in advertising.

Then government officials and consumer agencies begin to protest. Their protests first offend the advertising and publishing industries which cloak themselves in outraged virtue. But the agitation continues. Advertising agencies and publishers propose self-censorship, and tentative steps are taken. The consumers and government officials continue in hot pursuit. Legislation impends. Alarm increases. Advertisers and publishers swear by all that is holy they will be good.

It must not be forgotten that the advertising profits menaced are enormous and that any one of us views with alarm what appears to be an attack upon his own source of livelihood. In 1937 as many as 348 advertisers spent more than $100,000,000 on magazine, radio, and farm journal advertising, while 44 spent more than a million each. The grand total was $200,382,209. It cost $528,360, for instance, to advertise Anacin, $161,761 for Bisodol, $317,279 for

Kolynos Dentifrice, $195,894 for Ironized Yeast, $534,409 for Lysol, $1,021,362 for Fleischmann's Yeast, $220,030 for Kreml Hair Tonic (all hair tonics are by nature scientifically dubious) and $160,773 for Dr. Edwards Olive Tablets. (*Printers' Ink*, Jan. 27, 1938.)

Most of the products named are superfluous. Some are worse. All use or have used exaggerated or misleading advertising. The Food and Drug Administration or the Federal Trade Commission has at one time or another taken action against practically every one. But the advertising and newspaper and magazine publication industries, not to mention the radio, depend heavily upon them. Hence it was quite natural for a representative of the Thompson-Koch advertising agency to misrepresent Dr. Tugwell's position before the Proprietary Association in October, 1933. This Association then represented about 80 per cent of the packaged-medicine interests. This speaker generally derided the "Tugwell Bill," as he called it, and burlesqued its features. He dealt in misleading innuendo throughout and often deviated into real misrepresentation. (*Printers' Ink*, Oct. 19, 1933.)

Similarly the editor of *Food Industries* told the American Institute of New York that the proposed bill gave to the Secretary of Agriculture despotic power of life and death over the food, drug, and cosmetic industries, there being no appeal from the Secretary's decision. He added that "the manufacturer is again denied the right of appeal to the courts of justice for judicial relief." Nothing could well have been much further from the truth, as a reading of the proposed bill proved, but the statement had wide circulation in propaganda.

John C. Sterling, vice-president of McCall Co., condemned the bill in the February, 1934, *Forum-Century* and evolved the comforting doctrine that women consumers really enjoyed being fooled by advertising—though he also illogically insisted that "people are rarely fooled by even the most picturesque of advertising"—leaving the implication that women are not people! He declared that the bill would injure consumers, while formula disclosure would ruin food, medicine, and cosmetic manufacturers.

While, on the one hand, he contended that private brands and trademarks protected the most valuable of products, on the other hand he indicated that anyone could easily manufacture the same products once the formulas were disclosed. The housewife and the ordinary consumer had so long been guided by advertising state-

ments that rigid truth in advertising would confuse and perplex rather than aid them. If advertisers were curbed by law, held Sterling, the market would have vastly fewer cures on it—to great consumer disadvantage.

Charles Coolidge Parlin, manager of Commercial Research for Curtis Publishing Co., explained he opposed the bill because it rendered quality food standards mandatory. Wm. P. Jacobs, general manager of the Institute of Medicine Manufacturers, argued that to diminish advertising returns was to court disaster for "advertising furnishes the hope, the ambition, the forward look of business" and "printing alone represents approximately a 2 billion dollar industry, and we think we are safe in saying that three-fourths of this industry in some way or other is dependent upon commercial advertising." (Both articles in *Advertising & Selling,* Jan. 18, 1934.) This is revealing, coming from such a source.

Frank A. Blair, president of the Proprietary Association, called a revised law unnecessary. (*Editor and Publisher* for October 7, 1933.) He accused Tugwell of writing that advertising and sales effort represented economic waste, which was untrue, as can be seen by consulting Tugwell's *Industrial Discipline.* This was attested by an editorial quotation in the same issue of the same journal, wherein Tugwell was quoted as admitting that calling attention to new goods and services was always necessary, though "persuading customers to buy a dozen different articles of precisely the same uses and qualities is undiluted social waste."

Blair also repeated the myth that the bill would deprive the public of the right of self-medication. He added that it would destroy the proprietary industry, which it could not have done. He repeated the false statement that the law would establish Government dictatorship in this field, complained because it would not permit manufacturers to label a laxative as a cure for constipation, and denounced the bill as a "nuisance law" destined to upset the trend of business improvement under the New Deal.

Since Blair had written elsewhere (*Oil, Paint & Drug Reporter,* Oct. 9, 1933) that "the printing of a formula and warnings on the label will not prevent the purchaser from taking a remedy," his fears for the survival of the patent medicine industry appear unfounded according to his own testimony. Blair also claimed that all know there were few drug specifics for disease, though very few

actually know this, simply because "patent medicine" advertising has so consistently misinformed them.

Turning to the magazines proper we find all sorts of misrepresentation going on in the advertising pages of the *Woman's Home Companion* for March, 1934, the editor of which consistently opposed the Copeland Bill's passage. We find *Good Housekeeping* for December, 1933 (p. 90) congratulating itself upon its long advocacy of pure foods and honest advertising, and its advertising pages simply littered with false and misleading statements about various products, some of which had the seal of approval of its Institute, in the face of action by branches of the Federal Government proving they deserved no such seal.

In the October, 1933, issue of *Good Housekeeping* Dr. Walter H. Eddy endorsed the Copeland Bill in no uncertain terms, but an editorial in the December issue hastened to explain this away as an "endorsement in principle" only, and in the expectation that the bill would be greatly changed (emasculated) before passage. Furthermore advertising man Ernest Elmo Calkins was author of an article in this December issue wherein the bill was given "another look" and found objectionable.

While Walter G. Campbell (then chief of the Food and Drug Administration) and Tugwell were both admirable men, able and sincere, it would not be well thus to wipe out much of the patent medicine industry at one sweep, and it would be a real hardship to have to get a physician's prescription to buy aspirin and sodium bicarbonate—a silly piece of mendacity. The notions that the bill conferred supremacy over law to the Secretary of Agriculture and that advertising had educated us, were also rehashed. Of course advertising should always be "believable" and a "trustworthy buyer's guide," *which it decidedly was not* in that very issue of *Good Housekeeping*.

The Country Gentleman for February, 1934, ran a lead editorial entitled "A Bad Bill for Farmers," in which it was contended that a "good cause" had been used to cloak very dangerous legislation though, of course, "everyone wants proper safeguards against being sold something by misrepresentation." But the bill was said to have been designed instead to disorganize an important part of the machinery for marketing farm products! Food grades would be established, food labels would become truthful, a vast bureaucracy would arise, advertising would be put in a straight-jacket—"robbing it of all ap-

peal to the imagination," and the market for farm products would collapse. The same issue contained false, misleading, and wholly objectionable advertising of various remedies. (See Chapter XV, Harding's *Popular Practice of Fraud.*)

But, by November 23, 1933, *Printers' Ink* and advertising specialists generally foresaw that some sort of new law was inevitable. G. A. Nichols wrote therein asking opponents of the bill to "stop pawing the air, therefore, quit calling names, and refrain from shouting that the industries involved are too much regulated now and want no more regulation." Instead let them get together and give Government constructive suggestions.

The suggestions made thereupon left advertising the right to deceive by inference or ambiguity, exempting publishers and advertisers from liability for untruthful advertisements. They reserved to the patent medicine men the right to say what was a palliative and what a cure, to recommend specifics for certain diseases which doctors hold it dangerous to self-medicate, to market remedies in lack of scientific proof of their efficacy and harmlessness, and urged advertisers to admit their small inquities and purge themselves thereof. Advertisers should be warned first when naughty, not dealt with summarily, and no penalty should be inflicted unless repeated warnings failed.

In its issue for February 15, 1934, *Printers' Ink* officially endorsed and accepted the Copeland Bill, though the National Publisher's Association was reported still protesting over certain of its provisions. This was quite a contrast to G. A. Nichols' article in the same magazine, November 2, 1933, entitled "Beat the Tugwell Bill!" wherein all the old propaganda in this connection was rehashed and the further totally unsubstantiated charge was made that the American Medical Association had written the bill. The keynote then was "Advertising opinion should rule as to what should or should not be said about the product advertised."

We may conclude this section with the final blast at "The Menace of Tugwellism," which appeared in *Better Homes and Gardens* for February, 1934, at the time when the leading organ of the advertising industry had capitulated as noted above. This was signed "The Editors." Tugwell was described as a nice gentleman but a despot and a bureaucrat of the worst sort. The legislation he was sponsoring was dangerously seditious, illegal, menacing to business recovery and reemployment. It would destroy *all* proprietary drugs and

medicines, many cosmetics, and a large number of valuable food products. It would be enforced by tyrannical and oppressive methods!

Of course "the present Food and Drugs Act, enacted in 1906, needs strengthening. We are just as much in favor of abolishing fake remedies, and impure and dangerous foods, drugs, and cosmetics, as is Professor Tugwell or any of his associates. Our own policy of rigid advertising censorship proves this." A mere glance at the advertising section of the same issue revealed to the knowing eye a dozen advertisements of dentifrices, remedies, cold cures, and such, *each and every one of which was false and misleading or both.* (Cf. Harding's *Popular Practice of Fraud.*)

4. *The Quacks and Charlatans.* Analysis of propaganda emanating from this group need occupy but little space. Their ends and aims are obvious. In some instances they are sincere addicts to false or fantastic medical doctrines, or to fads and fancies of a quasi-therapeutic nature. Insofar as they were drugless healers they were inclined to support any measure that appeared to impede the manufacture and sale of drug products. Insofar as they themselves manufactured curious combinations of drugs and herbs, medicated foods, or quaint devices, they feared injury to their business and opposed the bill. Many of them widely propagandized their support or opposition in print and orally. This undoubtedly had weight with their followers. But again self-interest predominated and the attitude assumed was a mere reflection of the anticipated effect of the proposed legislation upon their commercial or therapeutic activities.

5. *The Medical Profession.* Organized physicians also had a natural self-interest in the passage of a new law to regulate patent medicines. In the nature of things they could not be altogether disinterested in their support of such legislation. This holds in spite of the fact that many reputable physicians, just like many well-qualified scientists in the field of pharmacy and in fields related to medicine and pharmacy, disinterestedly advocated better food, drug, and cosmetic legislation.

But the organized medical profession had and has specific interests of its own. It would like to see charlatanism and quackery eliminated. It would prefer a bill to abolish the right of unqualified healers to operate, and which would, if possible, eliminate chiropractors, osteopaths, nature healers, faith healers, and members of less orthodox medical cults and sects from practice altogether. Though

it admits the necessity for a certain amount of self-medication, it generally frowns upon this. It desires higher standards of medical practice and a great reduction in the number of patent medicines—other than ethical proprietaries or doctors' patent medicines.

It may in general be said that while the profession did not start the agitation for a new law, and certainly did not write it, doctors tended to support a more rigid form of drug regulation. Important officials of the American Medical Association offered invaluable aid to this end, although the association as an organization inclined to be hypercritical regarding each bill offered and never gave more than qualified endorsement to any.

In the December 9, 1933, issue of the *Journal of the American Medical Association* there will be found such an endorsement in an editorial. It argued there was necessity for some curb on advertising, as was indicated by the growth of private testing and certification agencies. Among these are the councils of the American Medical Association which test and certify the advertising statements of many food and drug products. The journals of the association later print the advertisements of products meeting its own councils' specifications. The association has a commercial self-interest here.

The editorial mentioned denounced the insinuations that the association had ever wanted self-medication abolished and that the bill prohibited such self-medication, which it did not. The American Medical Association recognized the usefulness of household remedies and had listed in its magazine *Hygiea* those it considered useful for the family medicine chest. But the person who treats himself should not be permitted to endanger his health and he should not be defrauded.

In this same issue of the *Journal* a doctor reported a fatal case of cirrhosis of the liver caused by a rheumatism remedy called "Renton's Hydrocin" which was one-half composed of the dangerous drug cinchophen. Three such fatal cases had been reported earlier in the *Journal*. The Bureau of Investigation of the American Medical Association had denounced these tablets January 17, 1931. They were then called Renton's Rheumatic Tablets. Earlier passage of legislation like the Copeland Bill would have prevented such fatalities.

It also would have prevented the catastrophe precipitated by the "Elixir Sulphanilamide," so called (it was not an elixir) put out by Massengill of Bristol, Tenn. The full story of this may be found in a

Report made to the Senate (Document No. 124, 75th Cong., 2nd Sess.) by the Secretary of Agriculture in 1937. This tragedy caused Dr. Henry Christian to write in the *New England Journal of Medicine* for January 13, 1938: "A medical profession that does nothing toward better laws for pure food, drugs, and cosmetics is assuming responsibility for other deaths likely to occur under present laws. That people have died from using Elixir Sulphanilamide is a challenge to physicians."

Broadly speaking, however, the medical profession worked comparatively disinterestedly for better patent medicine regulation, although its strict legalists were reluctant to endorse any proposal wholeheartedly, and inclined to find serious faults in every bill proposed.

6. *The Putative or Self-Appointed Consumer Friends.* In a sense all groups and individuals opposed to better food, drug, cosmetic, and advertising regulation expressed themselves as heartily in favor of increased protection for the consumer. This was obligatory because consumers had made themselves felt as a pressure group. But the groups classified here under putative consumer friends consisted of those comprising organizations which purported to examine and to certify the quality of goods on the American market for a subscription price or a fee—institutions like Consumers' Research.

First of all it must be remembered that these are primarily business or commercial organizations which advertise in much the same way that so called "unscrupulous" manufacturers do. They use what is commonly called "hell-fire" advertising, designed to frighten consumers into joining. They also freely use advertisements that tell nothing, but excite curiosity. Much of this publicity is usually embodied in books and articles of dubious accuracy and marked sensationalism. Nevertheless Consumers' Union is said to have reported expenditures of $34,091.04 for promotion in the fiscal year 1936-7 of which $19,854.79 went for advertising. Since the total expenses including salaries of technicians and all were but $17,307.71, and outside tests and laboratory expenses were but $10,780.25, it is obvious the union thought reasonably well of paid advertising. (*Printers' Ink*, Nov. 25, 1937.)

During that year Consumers' Union took in $122,055.12. Consumers' Research also had a decent income of some sort. This is fairly big business which, if "not operated for profit," does offer a very decent livelihood to its promoters. Moreover, given the best

intentions in the world, the officials of such organizations could not look with absolute calm upon the passage of legislation which, when strictly enforced, might encroach considerably upon the field of giving consumers information for a fee. Of course, in the nature of things, and given the speed with which new products and devices flow to the American market, it is technically impossible for any such organizations to assay them all critically, and to print the appraisals rapidly and fully enough to do much real good. Their problem is inherently incapable of solution by the means utilized.

Nevertheless the very appearance of such institutions was a portent. It meant that consumers were otherwise able to secure too little factual information regarding the products they purchased. These consumer organizations arose because there appeared to be need for them. But, when it came to a revision of the Food and Drugs Act, they proved to be doubtful friends to consumers.

Consumers' Research arrogated to itself credit for the suggestion of a new food and drugs act, attributing this in main to a singularly inaccurate, prejudiced, and sensational book published by two of its officials. (Consumers' Research *General Bulletin,* July, 1933). Yet the officials of the Food and Drug Administration had been clamoring for a stronger law that gave increased consumer protection ever since 1917. The then Chief of the Administration, Walter G. Campbell, had been especially insistent on this subject now for a decade, while Consumers' Research only got started on the subject in 1930.

On the other hand *100,000,000 Guinea Pigs,* however inaccurate factually and however biased, did serve to stir opinion. But the suggestions made therein for revising the Federal Food and Drugs Act had been made in 1917 by Dr. Carl L. Alsberg, then in charge of enforcement. Consumers' Research consistently berated government officials as sold out to business interests and declared that both Federal and State officials refused advice from "competent, disinterested, and unbiased technologists," like that of Consumers' Research. In their charges they were both biased and misleading. (Cf. Chas. D. Howard, *Health,* published by New Hampshire State Board of Health, issue for May, 1933.)

Consumers' Research was also urgent in putting forward various ideal food, drug, and cosmetic bills. These bills were consistently such as it would have been absolutely impossible to have enacted under existing conditions. Not only were their requirements ultrastringent,

but their enforcement would have required new employees and enlarged funds in such amounts that no Congress would approve. Essentially what these consumer organizations did was to protect their own private field of endeavor by putting forward legislation of such ultra-perfection that it could not possibly be passed.

Next they demanded revision on their own terms or none at all. As *The Nation* for May 2, 1934, remarked: "If the Tugwell bill fails of passage at this session of Congress, (which it did) as now seems quite likely, the responsibility will not rest entirely on the aggressive lobby maintained by the manufacturers of food, drugs, and cosmetics. Some of that doubtful distinction should go to certain self-styled 'liberals,' including Messrs. Kallett and Schlink, authors of *100,000,000 Guinea Pigs,* who are conducting an active propaganda against the measure on the ground that it is not perfect."

The measure was not perfect, of course. Neither did it pass then. It did not pass until June, 1938, for that matter. But such units as Consumers' Research did much by this subtle form of opposition to prevent the passage of a better law. In refusing to accept anything less than perfection they both gave Congress the impression that consumers and consumer friends were far from unanimous in their desires, and managed to protect their own business which would, in considerable part, have been obliterated had a really stringent, consumer-protective law been passed.

7. *The Real Consumer Friends.* There were certain groups and individuals who, insofar as it is possible to decide, did disinterestedly stand by the consumer. Some of them were misinformed by such pseudoliberal propaganda as was discussed above and therefore often turned out to be hindrances rather than aids. But many of them were alert, intelligent, well-informed, and capable of analyzing the varied propagandas for themselves. Among these were many individual physicians, pharmaceutical chemists, sociologists, economists, state and federal Government officials, scientists of sorts, and so forth.

Women also, both as individuals and as organized groups, steadily campaigned for a revised and stronger drug law. Associations of home economists, leagues of women voters, women's university clubs, and various women's groups made it plain that their outlook and philosophy differed markedly from what the editors of women's magazines appeared to think it was. Certain periodicals which carried little advertising—*The Nation, The New Republic, The Commonweal, Sat-*

urday Review of Literature, North American Review, Scientific American, and *The Christian Century,* for instance, carried many articles favorable to a revised and strengthened food and drugs act, though it was all but impossible to get magazines supported by advertising to print such articles.

8. *The Politicians.* The politicians were rather a factor in than an actual source of very active propaganda. It was difficult to find legislative sponsors for such legislation as is embodied in a really strong food and drugs act. Such legislation offers little opportunity or incentive to a politician interested in getting ahead. It was quite easy to find sponsors for amendments that would emasculate the stronger bills if they came to the floor of the Senate or House, or for bills that would tend to allay consumer agitation, but really without giving them markedly improved protection. Therefore S. 1944 and S. 2000 had little strong political support.

Any sponsor, of course, took upon himself an unpleasant task. Not only was he likely to lose the friendship of powerful manufacturers and advertisers in his state, but he would likewise be belabored as a shady and devious politician, ready to sell out to the "interests," by such pseudoliberals as the false consumer friends. In the nature of things the politician who sponsors any bill must first make it overstrong, so that he can later seem to emasculate it in order to satisfy colleagues in the opposition. We all know that legislation is always enacted through a series of trades effected among the legislators. (Cf. *New Republic,* Jan. 17, 1934, p. 264 for instance.)

In short, the politician in such cases always faces a large number of groups and individuals, each one demanding precisely the kind of regulation it desires and on its own terms. This acts as effectively as direct opposition when the bill itself is of such character as to afford the politician little opportunity to use it to advance himself and his own interests.

While manufacturers of all degrees of ethics, and the lack thereof, agreed that there should be better advertising and drug regulation, the emergency Conference of Consumer Organizations (numbering among them George Soule, Harry M. Laidler, Robert Morse Lovett, Elizabeth Gilman, and Freda Kirchway) demanded, because "the original Tugwell Bill was far too weak to afford adequate consumer protection, and the Copeland-revised bill is so much weaker from the

consumer viewpoint—that it be thrown out entirely and new legislation substituted." (Press of Feb. 26, 1934.)

Senator Copeland, the bill's sponsor, was also denounced as an unfit agent for the presentation of this legislation. This ignored two important facts, the first being that you simply cannot get anywhere by scrapping a piece of incipient legislation over which committees have worked for months to a basis of some agreement, and starting fresh. For you then have as far to go as at first. Secondly, whatever a particular senator's seeming ethical insensitivity to such matters as his appearance on a yeast program, he may be the sole regular Democrat in the Senate with a willingness, and with sufficient technical training, intelligently to sponsor the bill.

Senate liberals who might have found the bill emotionally congenial either lacked technical training, were not orthodox members of the party in power, or simply were busy with other matters they deemed more important. It would be hopeless to have such a bill in charge of a liberal who lacked all specialized knowledge and qualifications—just because his heart was in the right place and he was devoted to the public welfare. It is necessary under our system of government to utilize the best possible mechanism to secure the best possible legislation we can get enacted at any particular time.

Sponsoring a bill to regulate drugs and advertising rigidly is a thankless task for any politician. Certainly an extremely drastic bill, such as the putative consumer friends and pseudo-liberals desired, would have had no chance of passage. Practically nothing can be accomplished by simply abandoning a compromise bill and starting all over, especially when the compromise is, as this one was, stronger than the existing law and deserving of support. Nor can politicians be blamed for turning away from the "public good" and seeming to "sell out to the interests," when consumers deliberately confuse them and render their task doubly difficult.

9. *The Government Officials.* During all this time some propaganda was carried on by Government officials, especially those in the Federal Food and Drug Administration, which produced the exhibit of dangercus drugs and cosmetics popularly called "The Chamber of Horrors." Later, when the public was really aroused, and it seemed probable some new legislation would result, officials of the Federal Trade Commission stepped in seeking to reserve regulation of general advertising for themselves.

Despite the fact that ostensible consumer friends had long derided government officials for being timid and lethargic in asking new legislation, it is relatively unwise legally for them to attempt this. It might be construed as an attempt to influence Congress in favor of increased appropriations over the head of the Executive, who is legally charged with making fiscal recommendations. Nevertheless many of the officials did carry on an active propaganda for a better law.

This was for a variety of rather complex reasons. Some of them were purely selfish. Times had changed so that the old law was difficult to enforce; the officials wanted a law that would facilitate enforcement and make for greater efficiency. Again, they were responding quite naturally to increased pressure by consumers. They saw all about them outstanding abuses against the public health and pocketbook that they could not control.

The old 1906 law authorized no control over cosmetics, none over statements made in general advertising (it covered labels only), none over mechanical devices and other agencies for the correction of abnormalities that were not, strictly speaking, diseases. Worse still, it compelled the Government to prove not only that a label statement of therapeutic efficacy was false, but that it was fraudulent—i. e. was placed on the label with deliberate intent to defraud purchasers.

The bill under consideration would have remedied these and many other abuses. The officials, in order to speed its enactment, tried to be all things to all men: To assure politicians that it would not damage them to sponsor the bill, to insist to advertisers, manufacturers, and patent medicine men that the bill would only prohibit "untruthful" advertising and clear out their more objectionable competitors, to lead consumers to understand that the bill would give them full protection, to counteract the propaganda of putative consumer friends, to placate the medical profession, and to enlist support wherever possible.

Meanwhile, not only were two Government institutions disputing as to which should regulate advertising—the Food and Drug Administration and/or the Federal Trade Commission—but there were also natural differences of opinion among officials themselves. They were not in precise agreement as to just what kind of law would be best. The legal staff might hold one thing, the chemists and pharmacists

something else, while the administrative staff knew that certain provisions unconsidered by either were expedient.

In consequence, the officials appeared at hearings, made addresses, answered objections, explained provisions of the various bills, and combatted propaganda with counterpropaganda. Various articles and expositions were issued in mimeographed form. The radio, the motion picture, and horrible exhibits were all utilized. Doubtless the horrors were exaggerated as to effects and frequency, in some instances. All this is necessary in the formulation and control of public opinion in order to determine certain ends. (See *Printers' Ink,* Nov. 30 and Dec. 7, 1933, articles by Walter G. Campbell and by Chester M. Wright for examples of this propaganda.)

In general, the officials either presented the evils which they could not control under the existing law or else sought to deny some of the more mendacious statements made by those in opposition. They acquainted the public directly with the fact that it lacked protection in many fields, citing products by name. They endeavored to show that the proposed bills did not prohibit self-medication, did not give the officials dictatorial powers, and did not interfere with the business of either "honest" advertisers or "scrupulous" manufacturers who were, they contended, in majority. They tried to prove that passage of the bill would be good for business, while they denounced the "unscrupulous" individuals and organizations who opposed.

The culmination of this propaganda appeared in the above-mentioned *Report on Elixir Sulphanilamide* presented to Congress by the Secretary of Agriculture under date of November 26, 1937. Herein the tragedy was recited with marked restraint and maximum respect for verifiable facts. The manner in which the preparation had been made, using lethal diethylene glycol as a base, and the manner in which it was marketed without being tested, was all explained. The tragic results were given in some detail, along with an account of the producing company's pious assertion that it was sorry, but it had broken no law.

Nevertheless a few simple tests, or even a careful search of the scientific literature, would have disclosed to the maker—Samuel Evans Massengill, M. D., that the preparation was potentially very harmful. But the company's salesman said their customers wanted a liquid preparation of sulphanilamide, and this toxic liquid was the company's answer to their pleas. Had it been labeled a "solution" in-

stead of an "elixir" seizure would have been impossible legally, in spite of the nearly 100 deaths attributed to its use. For under the existing law a substance could not be seized and removed from the market merely because it was imminently dangerous to health and life. This mixture was seized because it was not, as branded, an elixir.

In the light of these facts the following recommendations were made to Congress:

1. That there be set up license control of all new drugs under guidance of a board of qualified experts, the same to apply also to combinations of well-known drugs not as yet found safe in combination, and to those bearing label directions for higher or more frequent dosage, or for use over a longer period, than is known justifiable. For doctors, dentists, pharmacists, steam fitters, electricians, and plumbers must be licensed; why not manufacturers of medicines? Why should they not also be technically qualified and fully educated?

2. That dangerous drugs be prohibited, this applying also to drugs or to drug combinations that may become dangerous if administered according to the manufacturer's directions. Many such are on the market today and cannot be seized legally.

3. That there be full and specific directions for use on the labels of all drug products, as well as warnings against misuse, overdosage, administration to children, or regarding use in conditions for which the product is not properly indicated.

4. That labels of medicines and remedies disclose the full formulas of the contents, thus abolishing secret remedies. Many drug products manufactured in the United States must bear this full formula declaration when sold abroad and are so packed and labeled for export. Why are Americans denied information given to foreigners? Symptoms are often produced in self-medicated patients by the remedies they take; these baffle physicians later called upon to diagnose their ailments. Label declaration of composition may often mean the difference between life and death when it fully informs physicians as to the exact drugs a patient has taken before consulting him.

Not all these recommendations were carried out, but a good Food, Drug, and Cosmetic Act was passed and approved, and it has since been strengthened. Meanwhile the Wheeler-Lee Act had already been passed, and the Federal Trade Commission proved far more vigilant in its enforcement than certain interests imagined who anticipated

that its control of advertising might be lax. The Commission and the Food and Drug Administration have not differed with one another so much that enforcement of their respective laws lagged. They cooperated closely and some former employees of the latter hold some key positions in the former.

But it is very interesting now, almost a decade later, to look back upon the highly misleading propaganda used by various individuals and agencies to aid and combat the passage of such legislation. There are too few accounts in the literature of such legislative battles. Their publication serves an excellent educational purpose. This account is necessarily limited too because only a book could do justice to the subject.

A RÉSUMÉ * OF SELECTED PAPERS PRESENTED BEFORE THE SCIENTIFIC SECTION OF THE AMERICAN PHARMACEUTICAL ASSOCIATION AUGUST 28-30, 1946, PITTSBURGH, PA.

A Photoelectric Colorimetric Assay for Digitoxin by Comparison With a Standard Powder

By A. E. James, F. O. Laquer and J. D. McIntyre

THE tentative plans for including digitoxin in the U. S. P. XIII prompted this investigation for an assay method that would avoid dependence on the expensive and difficult cat assay. A colorimetric assay was developed based on the Keller-Kiliani reaction. Briefly it is conducted as follows:

To samples of Digitoxin powder (Ladox Laboratories) containing 0.02 to 0.27 mg. were successively added 3 cc. of glacial acetic acid, 0.10 cc. of 5 per cent ferric chloride solution, and 0.25 cc. of concentrated sulfuric acid. The maximum color developed was measured in a Klett-Summerson Photoelectric Colorimeter. Data so obtained transcribed to a graph functioned as a standard reference curve. The digitoxin content of individual tablets, made by different manufacturers, were determined by extraction with chloroform, evaporation and treatment of the residue as was done with the powder. By reference to the standard curve values in close agreement with the labeled content were obtained.

The Colorimetric Assay of Digitoxin by the Raymond Method

By Robert C. Anderson and K. K. Chen

This was a second paper on the assay of digitoxin. The method employed was based upon the blue color produced when digitoxin is treated in dilute solution with *m*-dinitrobenzene and sodium hy-

* Based on official release from A. Ph. A. supplemented with notes taken at the meetings of the Section.

droxide. The color is then determined in a photoelectric colorimeter. The method although useful for determining the digitoxin content of tablets and ampuls is not specific enough to be used where admixture with other digi.alis glycosides exists.

A Study of Antacid Buffers. I. The Time Factor in Neutralization of Gastric Acidity

By James Holbert, Nancy Noble and I. W. Grote

The U. S. P. XII test for measurement of the acid consuming capacity of aluminum hydroxide gel and dried powder does not take into account the time required for acid neutralization, being simply a measure of excess acid neutralized after one hour. Since the patient using such tablets is perhaps equally interested in the rapidity of neutralization, a test was described in which a weighed amount of the antacid buffer is treated with artificial gastric juice and the pH rise measured at the end of one, five, ten, etc., minutes. Results were given when the test is applied to various types of liquid and dried aluminum hydroxide and similar types of buffers.

A Critical Investigation of the Amylolytic Activity of Pancreatin and Extract of Malt

By Charles W. Bauer and Algird John Raskauskas

The Lipolytic Activity of Pancreatin, U. S. P.

By Charles W. Bauer and Edwin E. Wilson

A Study of the Tryptic Activity of Pancreatin, U. S. P.

By Charles W. Bauer and Arthur K. White

The Carboxypeptidase Activity of Pancreatin, U. S. P.

By Charles W. Bauer and Alphonse M. Miskinis

This series of papers by Dr. Bauer and his associates reported a number of studies on the digestive powers of pancreatin and malt extract.

The amylolytic power of pancreatin was found to be far more dependent upon in appearance, i. e., lack of color, than its age. Both alpha and beta amylose were affected by the amylolytic enzymes of pancreatin and the type of starch used was unimportant. The starch paste employed, however, must be smooth, and homogenizing was recommended. The official definition should state the time involved in the assay which was recommended by the authors as five minutes for pancreatin and thirty minutes for extract of malt.

In investigating the lipolytic evaluation of pancreatin the authors developed a method using bentonite as a suspending agent for the fat and one which gave satisfactory results.

Pancreatin was found to contain a mixture of proteolytic enzymes, not a single one. The method given in the U. S. P. for preparing a casein solution was found unsatisfactory and it is recommended that the casein first be passed through a No. 100 sieve and that the finished solution be homogenized. The frequent claims for a particularly high potency trypsin are insignificant since many ordinary U. S. P. products were also at least three times the official standard of strength.

Pancreatin contains also the enzyme carboxypeptidase which is very stable, not being affected by either heat or formaldehyde. All pancreatins contain about the same amount. It is estimated by its digestive action on pumpkin seed globulin, the liberated amino acids being titrated with 0.02 *N* sodium hydroxide. The other enzymes are of course first destroyed by boiling.

Pharmaceutical Applications of Isopropyl Alcohol. I. As a Solvent in Pharmaceutical Manufacturing

By Doris Bullard Hawkins and Henry M. Burlage

The possibility of substituting isopropyl alcohol for ethyl alcohol led to this investigation. Isopropyl alcohol when administered orally was described as producing a euphoria similar to that experienced with ethyl alcohol but recovery requires more time than with ethyl alcohol.

Ten galenical preparations official in the U. S. P. XII and the N. F. VII were prepared with ethyl alcohol and with isopropyl

alcohol. Tables of comparison of the specific gravity, pH, color, odor, taste, changes on standing, and total extractive of the preparations were given. Tincture of Nux Vomica prepared with isopropyl alcohol contained a smaller per cent of strychnine when assayed by the U. S. P. XII method, but a higher per cent when assayed by the chromatographic method. Similar amounts of alkaloids were obtained in Tincture of Belladonna and Camphorated Tincture of Opium. Tincture of Hyoscyamus made with isopropyl alcohol contained a higher per cent of alkaloids than the tincture prepared with ethyl alcohol. In Tincture of Stramonium, the alkaloidal content was much lower in the isopropyl alcohol preparation, due to the very large amount of total extractive in the preparation.

Another paper by Dr. Burlage gave the solubility figures for twenty-seven local anesthetics in isopropyl alcohol at 25° C.

Penicillin Ointments and Creams

By M. L. Neuroth, Glenn L. Jenkins and C. O. Lee

A number of ointments and cream formulas containing penicillin were prepared and studied for their antibactericidal activity against organisms. Tests were made by a new modified agar cup-plate method which was devised in the laboratories of the School of Pharmacy at Purdue University.

The oil in water type of emulsion was found best as the vehicle for penicillin. Urea and sodium citrate were used to stabilize the penicillin. The authors submitted a number of formulas. One follows:

Cetyl Alcohol	21
Spermaceti	12.1
White Petrolatum	21
Sod. Lauryl Sulfate	0.3
Sod. Citrate	3.0
Urea	4.9
Sterile Water	37.7

Penicillin calcium was incorporated in the above base in an amount of 1000 units/Gm. It was suggested that since sodium lauryl sulfate is somewhat irritating to mucous membranes the use of non-ionic compounds might be a desirable improvement.

Availability of Penicillin From Various Ointment Bases

By H. A. Clymer and R. J. Ferlauto

Penicillin ointment employing an all grease base in compliance with the Food and Drug Administration monograph Section 146.26 shows inhibitory power when the ointment *per se* is tested by the standard agar plate diffusion method. This finding, together with the convenience as to stability, is believed to have led to the acceptance of all grease penicillin ointment as the standard form. The British employ formulas containing water quite generally as ointment vehicles for applying penicillin.

It is questionable whether this agar diffusion test gives adequate information to determine if the all grease preparation can fulfill the intent of topical application in yielding high local tissue concentrations of the penicillin. Insignificant amounts of penicillin on the surface of the ointment would be sufficient to yield zones of inhibition by the agar diffusion method while the large bulk of the penicillin would still be unobtainable.

The authors have studied the release of penicillin from various type ointment bases by methods which are believed to simulate more nearly actual *in vivo* conditions. A cellophane bag was used to test the diffusibility of the penicillin from the product. All grease bases were found quite inferior to emulsion type (O/W) bases in releasing penicillin. Data from these methods give actual concentration figures of the amount of penicillin released by the various type bases. Results obtained are proposed as the basis for a more rational means of choosing bases for penicillin to be used topically.

Water-containing formulas when refrigerated were found to lose 20 per cent of their penicillin content in one month and 50 per cent in two months.

Stability of Penicillin in Solutions of Ephedrine

By Victor P. Seeberg, Doris Jane Brown and Frederick F. Johnson

Reports on the treatment of sphenoethmoiditis with local penicillin therapy combined with spraying of a vasoconstrictor prompted a study of the stability of a combination of the two agents. Stability studies were conducted at 37° C., room temperature and refrigerator temperature on solutions of ephedrine sulfate with commercial sodium penicillin and commercial calcium penicillin. These were compared to a second series of similar penicillin solutions containing no ephedrine. The addition of ephedrine did not markedly alter the stability of penicillin in the concentrations tested. The solutions of penicillin with ephedrine were slightly less stable than those containing penicillin alone. Penicillin calcium plus ephedrine at room temperature lost 15 per cent of its penicillin in three days. Penicillin sodium plus ephedrine lost 15 per cent in twelve days. There was less deterioration at refrigerator temperatures.

A New Concept of the Role of Hydrogen Ion Concentration and Buffer Systems in Ophthalmic Preparations

By Harry W. Hind and Frank M. Goyan

These authors gave a very critical review of the whole subject of ophthalmic buffers. A number of interesting observations were made, e. g. alkaloids are most stable at low pH values but more active pharmacologically at higher pH values. It is necessary to selected optimum pH levels where both effectiveness and stability are maintained. The Gifford buffers were described as unstable. Boric Acid was recommended since it gives a stable product but one in which the pH of which rises rapidly when placed in the eye, thus increasing its activity. The authors classified ophthalmic drugs into five groups and described a buffer system recommended for the preparation of solutions in each group.

Note on the Pb Content of Solution Lead Subacetate, N. F.

By Donald C. Brodie and Amy Rasher

The National Formulary describes Solution of Lead Subacetate as a "clear" solution, with the added remark that the solution develops a "white precipitate" on exposure to air. This liquor is frequently a required laboratory preparation for beginning pharmacy students, and teachers usually permit but one or two filtrations, regardless of clarity, in order to minimize the formation of $PbCO_3$. Since the literature contains little or no information relative to the rate at which the total Pb content decreases with exposure to the air, several simple experiments were conducted to elucidate this point.

Eight 100 cc. samples of the solution were prepared by the N. F. hot and cold methods. Each solution was assayed three times for the total Pb content by the official method, the analyses being conducted on samples obtained from the filtrates after 1, 3 and 6 filtrations. Ordinary methods were used to prevent undue exposure to air. The filtrates after 1, 3 and 6 filtrations were slightly cloudy, slightly opalescent, and water-clear, respectively.

The mean Pb content for the eight samples in the two series were as follows: cold, 22.57, 22.31, 22.10 Gm./100 cc.; hot, 22.62, 22.50, 22.22 Gm./100 cc. The solutions were stored at room temperature and assayed at the end of two, four and six weeks. In the cold series the Pb content at the end of six weeks was 21.96 Gm./100 cc., whereas in the hot series the content was 22.31 Gm./100 cc.

Quaternary Ammonium Compounds as Preservatives

By L. F. Tice and A. W. Moore

The high bactericidal efficiency of the quaternary ammonium salts together with reports of their low index of toxicity led the authors to test their effectiveness as preservatives for protein and carbohydrate solutions. Gelatin solutions in varying concentrations and at both an acid and an almost neutral pH were used, as well as sucrose solutions and combinations of gelatin and sucrose. The anti-

septics employed were cetyl pyridinium chloride (Ceepryn) and *p*-tertiary octylphenoxyethoxyethyl dimethylbenzyl ammonium chloride (Phemerol). Each sample was inoculated with a culture of organisms previously grown on the nutrient material.

Very low concentrations of these antiseptics were found effective in preserving both gelatin and sucrose solutions alone, particularly at a pH range that precluded bacterial growth but not yeasts and molds. Combinations of gelatin and sucrose required much greater concentrations. Considerable difference in the efficiency of Phemerol and Ceepryn was found and a number of other interesting observations made.

Studies on Viburnum. II. A Comparative Study of the Sedative Effects of Extracts of Viburnum, Salicin and Saligenin Upon the Rat Uterus

By I. W. Grote and Maribelle Woods

A comparative study of the effect of various types of viburnum extracts and of salicin and saligenin was made on the rat uterus using the muscle chamber set up for posterior pituitary assay as laid down in the U. S. P.

Papaverine alkaloid was used as a reference standard. Considerable qualitative and quantitative differences in effects were obtained from the three drugs tested and the conclusion was reached that the major uterine sedative activity of viburnum extracts cannot be due to their salicin content.

Physiological Activity of Viburnum Leaves

By Rose P. Marriott and James C. Munch

Using various methods of bioassay, physiological activity has been established in leaves of various species of Viburnum, authenticated by Dr. Heber W. Youngken. Intravenously injected into dogs, alcoholic solutions of dried or fresh leaves showed significant depressor activity, from *V. prunifolium* or *V. cassinoides;* this action was not due to the alcohol content. By the isolated rat uterus technique, against papaverine, leaf samples have been as potent as

authentic *V. prunifolium* bark, N. F. The clinical activity of extract of authentic Viburnum leaves would appear to deserve clinical study.

Viburnum Studies: XIII. Uterine Potency of Extract of Viburnum Compared With Salicin and With Saligenin

By Rose P. Marriott and James C. Munch

The pharmacodynamic action of Salicin and of Saligenin differs from that of Viburnum Extract. Assays were made on the isolated rat uterus against papaverine hydrochloride. Salicin, while having a mild uterine depressant action alone, quantitatively decreased the uterine sedative response to Viburnum Extract administered alone. on the same uterus. Saligenin caused depression with a persisting lack of response to subsequent applications of itself or of Viburnum Extract, indicating some definite change in sensitivity of the tissue. By contrast repeated applications of Viburnum Extract of suitable strength produced substantially identical quantitative uterine sedation. It was concluded that neither Salicin nor Saligenin will produce the pharmacodynamic effects of Viburnum Extract by these tests.

Notes on the Pharmacology of Sodium Fluoroacetate

By Justus C. Ward

Results of extensive lethal dose studies on rats, mice, ground squirrels, prairie dogs, cats, bobcats, dogs, coyotes, badgers, guinea pigs, sheep, cattle, horses, chickens, hawks, eagles and other forms of life were presented. Sodium fluoroacetate is also known as 1080 and it is extremely poisonous, no antidote for it being known. The m. l. d. for the gopher is only 0.05 mg./Kg., for mice 1 mg./Kg. and for rats 8 mg./Kg. Dogs are very susceptible, the m. l. d. being 0.06 mg./Kg. One strange finding was that male ducks were twice as susceptible to it as females (males 7.5 mg./Kg.; females 16 mg./Kg.).

The problem of secondary poisoning is serious since dogs or cats eating a rat poisoned with it are likely to die. This is particularly

hazardous since the m. l. d. for dogs is only about 1/100th that for rats.

The mechanism of toxicity seems to vary from species to species.

Some Systemic Effects of Methergine

By Anton C. Kirchhof, Clay Racely and Nikanth M. Phatak

Methergine-Sandoz is the trade name for the synthetic ergonovine-like compound *d*-lysergic acid-*dl*-hydroxybutylamide-2. This compound was shown to have as marked uterine motor action as ergonovine, clinically to be effective in shortening the third stage of labor, without toxic or untoward side actions and, similar to ergonovine. It lacks the sympatholytic effect of ergotamine and ergotoxine [West, *J. Surg. Obs. Gyn., 52,* 197 (1944)]. Since all ergot alkaloids cause an increase in body temperature and mydriasis in rabbits, the authors were interested in determining if methergine had a similar action. Each of the following dosages of methergine were given intravenously to separate groups of three rabbits each: 0.4 mg./Kg., 0.8 mg./Kg., 1.6 mg./Kg. and 1.8 mg./Kg. For comparison, similar doses of ergonovine were given to another four groups of three rabbits each. Methergine produced an increase in body temperature and pupillary dilatation similar to, but not as marked as, ergonovine. In five normal human subjects given intravenous doses of 0.2 mg. of methergine in 1 cc. solution no appreciable changes in the pulse, blood pressure or respiration were noted when compared with five other subjects given 1 cc. doses of water placebos. It was concluded that the addition of one $-CH_2-$ in methergine, as compared to ergonovine, alters its pharmacologic activity slightly so that the new drug has a somewhat stronger motor uterine action and less pronounced systemic effects than ergonovine.

The Interaction of Sympathomimetic Pressor Amines: Inversion of the Vonedrine Pressor Action by Paredrine

By Raymond P. Ahlquist

The cardiovascular response to a sympathomimetic amine is always modified by the presence of a previous dose of the same or

another amine. The presser response may be increased or decreased or in some cases be inverted to a depressor action. This report is on a striking example of the last type of interaction.

The presence of paredrine [β-(*p*-hydroxyphenyl) isopropylmethylamine] in the anesthetized dog causes the pressor action of vonedrine (β-phenyl-*n*-propylmethylamine) to become inverted to a depressor action. Correlation of the arterial pressure and the rate of blood flow in the hind leg or head shows that this depressor action is due to peripheral vasodilation.

Repeated doses of vonedrine alone produce a diminishing pressor response but no depressor action appears. Other amines, including epinephrine, ephedrine, tyramine, sympatol and propadrine, do not invert vonedrine and are themselves not inverted by paredrine. Benzylimidazoline, a sympathomimetic anti-pressor agent, does not invert vonedrine.

The findings in this study indicate that the inversion of the vonedrine pressor response by paredrine may be an example of true reversal of action and not an unmasking of a normally present response. This effect is noticeable up to eight hours after the first drug is given.

A Study of the Toxicity of Two Isomeric Sodium Hydroxymercuribenzoates

By Thomas J. Haley and L. D. Edwards

Sodium hydroxymercuribenzoate has been recommended in a 1-5000 solution as an oral antiseptic (Hank's Antiseptic). The para compound is employed, the ortho isomer being less effective.

The LD_{50} (intraperitoneal) for sodium *p*-hydroxymercuribenzoate for rats was determined to be 5.0 mg./Kg. The LD_{50} (intraperitoneal) for sodium *o*-hydroxymercuribenzoate for rats was determined to be 15.5 mg./Kg. Chronic toxicity determinations following intraperitoneal injections in rabbits showed that both compounds were non-toxic under the conditions employed. Hematological examinations as a means of following chronic mercurial toxicity in rabbits yielded no results with the concentrations studied. An oral toxicity determination, employing the para compound in

the concentration suggested for a mouthwash, showed that the compound was non-toxic to rabbits even when given in large amounts.

The Evaluation of Antipyretics Against Pyrogen-Induced Fever

By Harold W. Werner and Marshall R. Warren

The subcutaneous injection in habbits of twenty times the threshold pyrogenic dose of a purified pyrogen prepared from *Proteus vulgaris* was found to produce a fever which persisted several hours. This fever was employed in evaluating antipyretic activity of aminopyrine, acetanilid, acetylsalicylic acid, and acetophenetidin.

Control rectal temperatures were obtained for a group of animals. Those with temperatures between 102.8° and 103.5° F. were subdivided into groups of six. The pyrogen solution was administered subcutaneously, and rectal temperatures were noted one and two hours later. Selected doses of antipyretics under test were then administered through a stomach tube; and rectal temperatures were followed for four hours at hourly intervals.

The amount of antipyretic required to arrest rise in temperature as well as the amount required to return it to normal was determined. The following figures were cited:

	Arrest	Return to normal
Aminopyrine	25-50 mg./Kg.	100 mg./Kg.
Acetanilid	100 mg./Kg.	200 mg./Kg.
Acetylsalicylic acid	200 mg./Kg.	200 mg./Kg.

200 mg./Kg. of aminopyrine caused a precipitous drop to about 3° F. below normal. A similar dose of acetanilide decreased rectal temperature to about 1° below normal. Acetylsalicylic acid reduced temperatures only to normal. Acetophenetidin failed to restore body temperature to normal even in 800 mg./Kg. doses.

Based on these results the order of decreasing mg. potency for the four compounds investigated is: aminopyrine, acetanilid, acetylsalicylic acid, acetophenetidin.

The Antibacterial Action of Dialkylaminoalkyl Ethers of Stilbestrol and Hexylresorcinol

By C. W. Chapman, G. P. Hager and D. E. Shay

The preparation of certain dialkylaminoalkyl ethers of stilbestrol and hexylresorcinol is described. The action of these compounds on *Staphylococcus aureus, Eberthella typhi* and *Mycobacterium tuberculosis* was discussed. The stilbestrol derivative used in these experiments appears to have little or no estrogenic activity.

The compound with hexylresorcinol was found to inhibit *Mycobacterium tuberculosis* in a dilution of 1-100,000. *Staphylococcus aureus* was killed in a 1-10,000 dilution in sixty minutes and *Eberthella typhi* was killed in a 1-50,000 dilution in sixty minutes.

On the Oxytocic Activity of Pitocin and Pitressin on Mammalian Uteri by a Graded Response Method

By W. M. Bachinski and M. G. Allmark

A graded response method of assay employing longitudinal strips of uterine muscle from the guinea pig, rat, rabbit and human were used for the study. The uterine muscle strips were excised at the normal, parturient, and postpartum states of the animal. For guinea pig and rat uteri, the pitocin to pitressin ratios were found to be quite similar, being approximately ten to one for the normal uterus and twenty to one on the parturient and postpartum uteri. On uterine strips excised from normal rabbits the oxytocic effect of pitressin was almost twice that of pitocin; in the parturient and postpartum states, however, the oxytocic effect of pitocin was found to be five times that of pitressin. On the human uterine strips excised from the lower uterine segment at the parturient stage, the oxytocic effect of pitressin was almost equal to that of pitocin.

There was observed a marked difference in the sensitivity of the various mammalian uterine strips to pitocin and pitressin. The range sensitivity of the rabbit and human uterine muscle strips, however, appeared to be the same.

The oxytocic potency of pitocin was found to be about the same on the normal rabbit and parturient human uterine strips but differed significantly from the normal guinea pig.

SELECTED ABSTRACTS

Effect of Some Sulfhydryl-containing Substances on the Toxicity of an Organic Mercurial Compound. W. K. Long and A. Farah. *Science 104,* 220 (1946). The following compounds containing the sulfhydryl group (—SH) were tested for antidotal action against the acute toxicity of the mercurial diuretic Salyrgan: cysteine hydrochloride, glutathione, 2,3-dimercapto-propanol (British anti-lewisite), cystine and methionine.

The intravenous administration of both cysteine hydrochloride and glutathione to mice one minute before the LD_{50} of Salyrgan was given by the same route was found to give the animals marked protection against the toxicity of the compound. Cystine and methionine offered only slight protection.

The toxic effects produced in the intact anesthetized cat and dog by a lethal dose of Salyrgan were found to be chiefly upon the circulation, and especially the heart. These manifestations were promptly counteracted by cysteine hydrochloride and glutathione (both in doses of 5-10 mg./Kg.) and by 2,3-dimercapto-propanol (0.5-2 mg./Kg.).

Experiments on the heart-lung preparation of the dog demonstrated that the severe heart failure produced by 150 mg. of Salyrgan can be readily counteracted by 100 mg. of glutathione, 56 mg. of cysteine hydrochloride and 10 mg. of 2,3-dimercapto-propanol.

Influence of pH and Temperature on the Survival of Coliforms and Enteric Pathogens When Exposed to Chloramine. C. T. Butterfield and E. Wattie. *Public Health Rep. 61,* 157 (1946). Data are presented on the bactericidal properties of the chloramines against species of *Escherichia, Aerobacter, Pseudomonas, Eberthella* and *Shigella,* supplementing similar reports made on the efficiency of free chlorine. The experiments were performed at pH 6.5, 7.0,

7.8, 8.5, 9.5 and 10.5 at two temperature ranges, *viz.*, 2° to 6° C., and 20° to 25° C., with various ratios of chlorine and ammonia nitrogen.

It was found that the rate of bacterial kills is primarily influenced by the amount of chloramine present and by the length of exposure of the bacteria to the bactericide. If the chloramine residual is about 1.2 p. p. m., an exposure of not less than twenty minutes is required to obtain a 100 per cent kill at pH 7.0 with a temperature of 20° to 25° C.

The bactericidal activity of chloramine was found to decrease as the pH increased. Under constant conditions of room temperature and concentration of chloramine (0.6 p. p. m.), an exposure of forty minutes at pH 7.0 was required for a 100 per cent kill; at pH 8.5, 120 minutes; and at pH 9.5, 240 minutes. In order to obtain a 100 per cent kill in forty minutes at pH 8.5, it was found necessary to increase the chloramine residual to about 1.5 p. p. m.

It was also noted that the bactericidal activity of chloramine decreased at lower temperatures. Thus, to obtain a 100 per cent kill at 2° to 6° C. it required either nine times as long an exposure period or a chloramine concentration 2.5 times as great as that necessary at 20° to 25° C.

The bactericidal properties of the chloramines were not altered by the length of contact time (0 to 68 hours) of the chlorine and ammonia used to produce them, nor were they markedly reduced by the presence of excessive amounts of ammonia nitrogen (Cl_2:N ratios of 1:25).

Chloramines were found to be much less efficient than free chlorine as a bactericide. To obtain 100 per cent kills in identical exposure periods, the chloramine concentration necessary was twenty-five times greater than that of free chlorine. With the same concentration of bactericide under identical conditions, the exposure period for chloramine was about 100 times that of free chlorine.

Sex Hormones. A. C. Frazer. *Pharm. J. 103,* 80 (1946). The sex hormones may be classified in three groups; the changes which they bring about at puberty are as follows: (1) estrogens, which are concerned with female secondary sexual char-

acteristics, menstruation, and ovulation; (2) androgens, which are concerned with male secondary sexual characteristics; and (3) progestins, which inhibit menstruation and ovulation and are also responsible for the changes in, and maintenance of, pregnancy.

All of these compounds have the same basic sterol structure, but differ in the substituent groups and in the extent of saturation of the nucleus.

It is believed that both androgens and estrogens occur in both sexes. The balance between the sex hormones is complicated by their relationships with the gonadotrophic hormones of the pituitary gland and with others, such as the adrenal and thyroid glands. A lack of balance between the various sex hormones and associated substances may cause profound changes on general bodily function; such signs of imbalance are frequently observed at the climacteric in both sexes.

Estrogens may consist of purified natural products of known composition, natural concentrates, or synthetic compounds. In general, esters produce an effect of greater duration than non-esterified compounds. Androgens are best administered parenterally as the synthetic testosterone propionate in oil. Progestins should be given parenterally as the synthetic progesterone in oil.

The author cautions that these potent substances should be used only with a full understanding of their pharmacological properties, especially since it is known that some of these compounds are carcinogenic, and that endocrine imbalance may produce serious results.

The Stability of Penicillin Solutions. R. Denston. *Pharm. J. 103,* 71 (1946). An investigation of the stability of "mega" packs of high potency penicillin (1280 i. u. per mg.) led to the conclusion that 90 per cent of its activity is retained after storage for five to six days either at room temperature or in the refrigerator, 85 per cent after ten to fourteen days in the refrigerator, and about 60 per cent after up to thirty-six days in the refrigerator. At room temperature, the half-life was about eighteen days.

Pure penicillin was dissolved in sterile phosphate buffer to produce a solution of pH 7 containing 100,000 i. u. per mil. The buffer solution contained 0.78 gm. of potassium dihydrogen phosphate and 1.0 gm. of dipotassium hydrogen phosphate per liter. Such a solution was stable toward storage in the refrigerator for the thirty-six day test period and had no significant loss of potency when stored at room temperature for fourteen days; after seventeen days there was a rapid loss, and after twenty-one days not more than 30 per cent of the original activity could be demonstrated.

No significant loss of potency occurred after boiling a solution of pure penicillin sodium in distilled water (20,000 i. u. per mil.) for five minutes. A similar solution containing penicillin of a 1400 i. u. per mg. strength lost 10 per cent of its activity after being boiled for five minutes, and over 90 per cent after boiling for ten minutes.

Studies made on the effect of antiseptics on the stability of penicillin solutions stored in the refrigerator for twenty-eight days indicated that phenoxetol (β-phenoxyethyl alcohol) 2 per cent, chlorocresol 0.1 per cent, and phenol 0.5 per cent did not produce an adverse effect. 5-Aminoacridine hydrochloride, chlorbutol and merthiolate decreased the stability. At room temperature phenol was the only antiseptic of the compounds tested which caused no significant loss of potency.

The addition of 30 per cent of glycerin to an aqueous solution of penicillin did not cause a significant loss of potency during storage in the refrigerator for five days, but thereafter the activity decreased more rapidly than in a control solution prepared with distilled water. At room temperature the half-life of such a glycerin solution was about three to four days.

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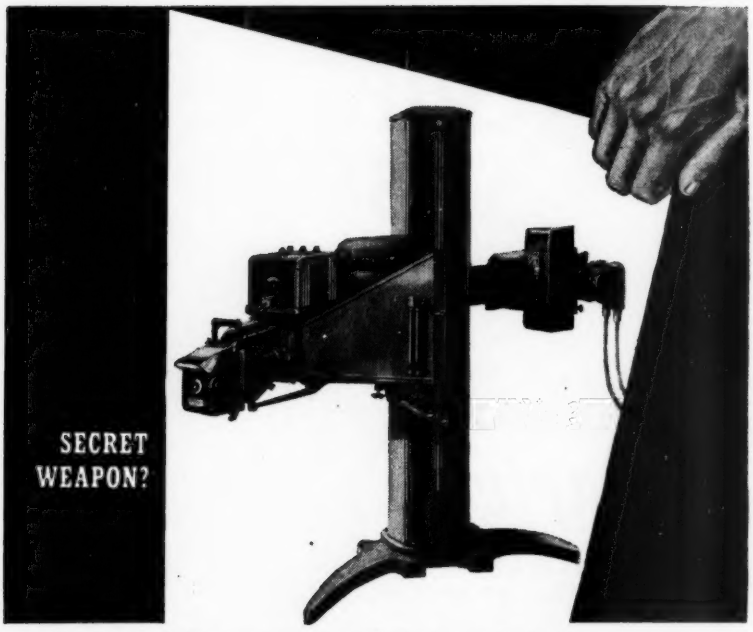

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